What is claimed is:

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1. A compound of Formula (I):

(I)

10 wherein:

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 R^1 is selected from the group consisting of hydrogen, halo, alkyl, haloalkoxy, cycloalkyl, heteroalicyclic, hydroxy, alkoxy, $-C(0)R^8$, $-NR^9R^{10}$ and $-C(0)NR^{12}R^{13}$;

 R^2 is selected from the group consisting of hydrogen, halo, alkyl, trihalomethyl, hydroxy, alkoxy, cyano, $-NR^9R^{10}$, $-NR^9C(O)R^{10}$, $-C(O)R^8$, $-S(O)_2NR^9R^{10}$ and $-SO_2R^{14}$ (wherein R^{14} is alkyl, aryl, aralkyl, heteroaryl and heteroaralkyl);

 ${\ensuremath{R^3}}$, ${\ensuremath{R^4}}$ and ${\ensuremath{R^5}}$ are independently hydrogen or alkyl;

Z is aryl, heteroaryl, heterocycle, or $-NR^{15}R^{16}$ wherein R^{15} and R^{16} are independently hydrogen or alkyl; or R^{15} and R^{16} together with the nitrogen atom to which they are attached from a heterocycloamino group;

 ${\ensuremath{\mathsf{R}}}^6$ is selected from the group consisting of hydrogen or alkyl;

 R^7 is selected from the group consisting of hydrogen, alkyl, aryl, heteroaryl, and $-C(0)R^{17}$ as defined below;

R⁸ is selected from the group consisting of hydroxy, alkoxy and aryloxy; R⁹ and R¹⁰ are independently selected from the group consisting of hydrogen, alkyl, cyanoalkyl, cycloalkyl, aryl and heteroaryl; or

 R^9 and R^{10} combine to form a heterocycloamino group; R^{12} and R^{13} are independently selected from the group consisting of hydrogen, alkyl, hydroxyalkyl, and aryl; or R^{12} and R^{13} together with the nitrogen atom to which they are attached form a heterocycloamino;

R¹⁷ is selected from the group consisting of alkyl, 10 cycloalkyl, aryl, hydroxy and heteroaryl; or a pharmaceutically acceptable salt thereof.

2. The compound of claim 1, wherein:

 R^1 is selected from the group consisting of hydrogen, 15 halo, alkyl, cycloalkyl, heteroalicyclic, hydroxy, alkoxy, $-C(0)R^8$, $-NR^9R^{10}$ and $-C(0)NR^{12}R^{13}$;

 R^2 is selected from the group consisting of hydrogen, halo, alkyl, trihalomethyl, hydroxy, alkoxy, cyano, $-NR^9R^{10}$, $-NR^9C(0)R^{10}$, $-C(0)R^8$, $-S(0)_2NR^9R^{10}$ and $-SO_2R^{14}$ (wherein R^{14} is alkyl, aryl, aralkyl, heteroaryl and heteroaralkyl);

 R^3 , R^4 and R^5 are independently hydrogen or alkyl;

Z is aryl, heteroaryl, heterocycle, or $-NR^{15}R^{16}$ wherein R^{15} and R^{16} are independently hydrogen or alkyl; or R^{15} and R^{16} together with the nitrogen atom to which they are attached form a heterocycloamino group;

 ${\ensuremath{\mathsf{R}}}^6$ is selected from the group consisting of hydrogen or alkyl;

 R^7 is selected from the group consisting of hydrogen, alkyl, aryl, heteroaryl, and $-C(0)R^{17}$ as defined below;

R⁸ is selected from the group consisting of hydroxy, alkoxy and aryloxy;

R⁹ and R¹⁰ are independently selected from the group consisting of hydrogen, alkyl, cyanoalkyl, cycloalkyl, aryl and heteroaryl; or

R⁹ and R¹⁰ combine to form a heterocyclo group; R^{12} and R^{13} are independently selected from the group

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consisting of hydrogen, alkyl and aryl, or R^{12} and R^{13} together with the nitrogen atom to which they are attached form a heterocycle;

R¹⁷ is selected from the group consisting of alkyl, cycloalkyl, aryl, hydroxy and heteroaryl; or a pharmaceutically acceptable salt thereof.

3. The compound or salt of claim 1, wherein the compound is selected from the group consisting of:

Cpd No.	Structure	Name
1N	Honor of the second of the sec	5-(5-Fluoro-2-oxo-1,2-dihydro-indol-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (3-diethylamino-2-hydroxy-propyl)-amide
2N	HOH NOH	5-[5-Fluoro-2-oxo-1,2-dihydro-indol-(3)-ylidenemethyl]-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-hydroxy-3-morpholin-4-yl-propyl)-amide
3N	H OH NO	2,4-Dimethyl-5-[2-oxo-1,2-dihydro-indol-(3)-ylidenemethyl]-1H-pyrrole-3-carboxylic acid (2-hydroxy-3-morpholin-4-yl-propyl)-amide
4N	CI HOH NOH	5-[5-Chloro-2-oxo-1,2-dihydro-indol-(32)-ylidenemethyl]-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-hydroxy-3-morpholin-4-yl-propyl)-amide
5N	Br H OH NO	5-[5-Bromo-2-oxo-1,2-dihydro-indol-ylidenemethyl]-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-hydroxy-3-morpholin-4-yl-propyl)-amide

6N H OH N=N

2,4-Dimethyl-5-[2-oxo-1,2-dihydro-indol-ylidenemethyl]-1H-pyrrole-3-carboxylic acid (2-hydroxy-3-[1,2,3]triazol-1-yl-propyl)-amide

5-[5-Fluoro-2-oxo-1,2-dihydro-indol-ylidenemethyl]-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-hydroxy-3-[1,2,3]triazol-1-yl-propyl)-amide

5-[5-Chloro-2-oxo-1,2-dihydro-indol-ylidenemethyl]-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-hydroxy-3-[1,2,3]triazol-1-yl-propyl)-amide

5-[5-Bromo-2-oxo-1,2-dihydro-indol-ylidenemethyl]-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-hydroxy-3-[1,2,3]triazol-1-yl-propyl)-amide

3-{[4-({[3-(diethylamino)-2-hydroxypropyl]amino}carbonyl)-5-methyl-3-phenyl-1H-pyrrol-2-yl]methylene}-2-oxo-N-phenyl-2,3-dihydro-1H-indole-5-carboxamide

(3-{[4-({[3-(diethylamino)-2-hydroxypropyl]amino}carbonyl)-5-methyl-3-phenyl-1H-pyrrol-2-yl]methylene}-N-methyl-2-oxo-2,3-dihydro-1H-indole-5-carboxamide

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(3Z)-3-{[4-({[3-(diethylamino)-2-hydroxypropyl]amino}carbonyl)-5-methyl-3-phenyl-1H-pyrrol-2-yl]methylene}-N-(2-hydroxyethyl)-2-oxo-2,3-dihydro-1H-indole-5-carboxamide

14N

N-[3-(diethylamino)-2hydroxypropyl]-4-(4fluorophenyl)-2-methyl-5-{[5-(morpholin-4-ylcarbonyl)-2oxo-1,2-dihydro-3H-indol-3ylidene]methyl}-1H-pyrrole-3carboxamide

3-{[4-({[3-(diethylamino)-2-hydroxypropyl]amino}carbonyl)-3-(4-fluorophenyl)-5-methyl-1H-pyrrol-2-yl]methylene}-N-isopropyl-2-oxo-2,3-dihydro-1H-indole-5-carboxamide

16N F HO HN O H

3-{[4-({[3-(diethylamino)-2-hydroxypropyl]amino}carbonyl)-3-(2,4-difluorophenyl)-5-methyl-1H-pyrrol-2-yl]methylene}-2-oxo-N-phenyl-2,3-dihydro-1H-indole-5-carboxamide

17N 18N

3-{[4-({[3-(diethylamino)-2hydroxypropyl]amino}carbonyl) -3-(2,4-difluorophenyl)-5methyl-1H-pyrrol-2yl]methylene}-N-(2hydroxyethyl) -2-oxo-2,3dihydro-1H-indole-5carboxamide

3-{[3-(4-cyanophenyl)-4-({[3-(diethylamino) -2hydroxypropyl]amino}carbonyl) -5-methyl-1H-pyrrol-2yl]methylene}-N,N-dimethyl-2oxo-2,3-dihydro-1H-indole-5carboxamide

4-(4-cyanophenyl)-N-[3-(diethylamino) -2hydroxypropyl]-2-methyl-5-{[5-(morpholin-4-ylcarbonyl)-2-oxo-1,2-dihydro-3H-indol-3ylidene]methyl}-1H-pyrrole-3carboxamide

20N

 $3-\{[3-(4-chlorophenyl)-4-$ ({[3-(diethylamino)-2hydroxypropyl]amino;carbonyl) -5-methyl-1H-pyrrol-2yl]methylene}-2-oxo-N-phenyl-2,3-dihydro-1H-indole-5carboxamide

144

19N

21N

CI HO

HN

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NH

23N

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24N F F N OH H OH

25N F H OH

3-{[3-(4-chlorophenyl)-4-({[3-(diethylamino)-2hydroxypropyl]amino}carbonyl) -5-methyl-1H-pyrrol-2yl]methylene}-N-isopropyl-2oxo-2,3-dihydro-1H-indole-5carboxamide

5-[(5-fluoro-2-oxo-1,2-dihydro-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(2H-tetraazol-2-yl)propyl]-2,4-dimethyl-1H-pyrrole-3-carboxamide

5-[5-chloro-2-oxo-1,2-dihydro-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(2H-tetraazol-2-yl)propyl]-2,4-dimethyl-1H-pyrrole-3-carboxamide

N-[2-hydroxy-3-(2H-tetraazol-2-y1)propyl]-2,4-dimethyl-5-{[2-oxo-5-trifluoromethoxy)-1,2-dihydro-3H-indol-3-ylidene]methyl}-1H-pyrrole-3-carboxamide

5-[(5-fluoro-2-oxo-1,2-dihydro-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(1H-tetraazol-1-yl)propyl]-2,4-dimethyl-1H-pyrrole-3-carboxamide

26N CI H H OH H

5-[(5-chloro-2-oxo-1,2-dihydro-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(1H-tetraazol-1-yl)propyl]-2,4-dimethyl-1H-pyrrole-3-carboxamide

27N FFF HAVE N H OH H

N-[2-hydroxy-3-(1H-tetraazol-1-yl)propyl]-2,4-dimethyl-5-{[2-oxo-5-trifluoromethoxy)-1,2-dihydro-3H-indol-3ylidene]methyl}-1H-pyrrole-3carboxamide

28N H OH OH

N-{3-[2,6-dimethylmorpholin-4-yl]-2-hydroxypropyl}-5-[(5-fluoro-2-oxo-1,2-dihydro-3H-indol-3-ylidene)methyl]-2,4-dimethyl-1H-pyrrole-3-carboxamide

CI NOH H

5-[(5-chloro-2-oxo-1,2-dihydro-3H-indol-3-ylidene)methyl]-N-{3-[2,6-dimethylmorpholin-4-yl]-2-hydroxypropyl}-2,4-dimethyl-1H-pyrrole-3-carboxamide

30N FFF H

N-{3-[2,6-dimethylmorpholin-4-yl]-2-hydroxypropyl}-2,4dimethyl-5-{[2-oxo-5-(trifluoromethoxy)-1,2dihydro-3H-indol-3ylidene]methyl}-1H-pyrrole-3carboxamide

146

29N

34N 35N 36N 37N 38N 39N

5-[(5-fluoro-2-oxo-1,2-dihydro-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(3-methyl-2,5-dioxoimidazolidin-1-yl)propyl]-2,4-dimethyl-1H-pyrrole-3-carboxamide

N-[2-hydroxy-3-(3-methyl-2,5-dioxoimidazolidin-1-yl)propyl]-2,4-dimethyl-5-{(Z)-[2-oxo-5-(trifluoromethoxy)-1,2-dihydro-3H-indol-3-ylidene]methyl}-1H-pyrrole-3-carboxamide

5-[(5-chloro-2-oxo-1,2-dihydro-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(3-methyl-2,5-dioxoimidazolidin-1-yl)propyl]-2,4-dimethyl-1H-pyrrole-3-carboxamide

N-[3-(1,1-dioxidothiomorpholin-4-yl)-2-hydroxypropyl]-2,4-dimethyl-5-[(2-oxo-1,2-dihydro-3H-indol-3-ylidene)methyl]-1H-pyrrole-3-carboxamide

N-[3-(1,1-dioxidothiomorpholin-4-yl)-2-hydroxypropyl]-5-[(5-fluoro-2-oxo-1,2-dihydro-3H-indol-3-ylidene)methyl]-2,4-dimethyl-1H-pyrrole-3-carboxamide

5-[(5-chloro-2-oxo-1,2-dihydro-3H-indol-3-ylidene)methyl]-N-[3-(1,1-dioxidothiomorpholin-4-yl)-2-hydroxypropyl]-2,4-dimethyl-1H-pyrrole-3-carboxamide

5-[(5-bromo-2-oxo-1,2-dihydro-3H-indol-3-ylidene)methyl]-N-[3-(1,1-dioxidothiomorpholin-4-yl)-2-hydroxypropyl]-2,4-dimethyl-1H-pyrrole-3-carboxamide

47N 48N 49N 50N 51N

5-(5-fluoro-2-oxo-1,2dihydro-indol-3ylidenemethyl) -2,4dimethyl-1H-pyrrole-3carboxylic acid [2hydroxy-3-([1,2,3]triazolo[4,5b]pyridin-3-yloxy)propyl]-amide 5-(5-chloro-2-oxo-1,2dihydro-indol-3ylidenemethyl) -2,4dimethyl-1H-pyrrole-3carboxylic acid [2hydroxy-3-([1,2,3]triazolo[4,5b]pyridin-3-yloxy)propyl]-amide 2,4-dimethyl-5-(2-oxo-5-trifluoromethoxy-1,2dihydro-indol-3ylidenemethyl) -1Hpyrrole-3-carboxylic acid [2-hydroxy-3-([1,2,3]triazolo[4,5b]pyridin-3-yloxy)propyl]-amide 5-(5-fluoro-2-oxo-1,2dihydro-indol-3ylidenemethyl) -2,4dimethyl-1H-pyrrole-3carboxylic acid [2hydroxy-3-(3-oxybenzotriazol-1-yl)propyl]-amide 5-(5-chloro-2-oxo-1,2dihydro-indol-3ylidenemethyl) -2,4dimethyl-1H-pyrrole-3carboxylic acid [2hydroxy-3-(3-oxybenzotriazol-1-yl)-

52N

propyl]-amide

2,4-dimethyl-5-(2-oxo5-trifluoromethoxy-1,2dihydro-indol-3ylidenemethyl)-1Hpyrrole-3-carboxylic
acid [2-hydroxy-3-(3oxy-benzotriazol-1-yl)propyl]-amide

4. The compound or salt of claim 3, wherein the compound is selected from the group consisting of:

Cpd No.	Structure	Name
18	NH OH N	5-(5-Fluoro-2-oxo-1,2-dihydro-indol-3-(3Z)-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (3-diethylamino-2-hydroxy-propyl)-amide
2S	P H OH NO	5-[5-Fluoro-2-oxo-1,2-dihydro-indol-(3Z)-ylidenemethyl]-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-hydroxy-3-morpholin-4-yl-propyl)-amide
3S	N H OH NO	2,4-Dimethyl-5-[2-oxo-1,2-dihydro-indol-(3Z)-ylidenemethyl]-1H-pyrrole-3-carboxylic acid (2-hydroxy-3-morpholin-4-yl-propyl)-amide
4S	CI NH OH NO	5-[5-Chloro-2-oxo-1,2-dihydro-indol-(3Z)-ylidenemethyl]-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-hydroxy-3-morpholin-4-yl-propyl)-amide
5S	Br H OH NO	5-[5-Bromo-2-oxo-1,2-dihydro-indol-(3Z)-ylidenemethyl]-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-hydroxy-3-morpholin-4-yl-propyl)-amide

2,4-Dimethyl-5-[2-oxo-1,2-dihydro-indol-(3Z)-ylidenemethyl]-1H-pyrrole-3-carboxylic acid (2-hydroxy-3-[1,2,3]triazol-1-yl-propyl)-amide

7S F H OH N=N

5-[5-Fluoro-2-oxo-1,2-dihydro-indol-(3Z)-ylidenemethyl]-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-hydroxy-3-[1,2,3]triazol-1-yl-propyl)-amide

8S CI H OH N=N

5-[5-Chloro-2-oxo-1,2-dihydro-indol-(3Z)-ylidenemethyl]-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-hydroxy-3-[1,2,3]triazol-1-yl-propyl)-amide

9S

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N=N
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OH
N=N

5-[5-Bromo-2-oxo-1,2-dihydro-indol-(3Z)-ylidenemethyl]-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-hydroxy-3-[1,2,3]triazol-1-yl-propyl)-amide

(3Z)-3-{[4-({[3-(diethylamino)-2hydroxypropyl]amino}carbonyl) -5-methyl-3-phenyl-1H-pyrrol-2-yl]methylene}-2-oxo-Nphenyl-2,3-dihydro-1H-indole-5-carboxamide

12S HN O

(3Z)-3-{[4-({[3-(diethylamino)-2hydroxypropyl]amino}carbonyl) -5-methyl-3-phenyl-1H-pyrrol-2-yl]methylene}-N-methyl-2oxo-2,3-dihydro-1H-indole-5carboxamide

11S

Attorney Docket No. 038602-1310

14S

15S

(3Z)-3-{[4-({[3-(diethylamino)-2-hydroxypropyl]amino}carbonyl)-5-methyl-3-phenyl-1H-pyrrol-2-yl]methylene}-N-(2-hydroxyethyl)-2-oxo-2,3-dihydro-1H-indole-5-carboxamide

HO HN O

N-[3-(diethylamino)-2-hydroxypropyl]-4-(4-fluorophenyl)-2-methyl-5-((Z)-[5-(morpholin-4-ylcarbonyl)-2-oxo-1,2-dihydro-3H-indol-3-ylidene]methyl}-1H-pyrrole-3-carboxamide

(3Z)-3-{[4-({[3-(diethylamino)-2hydroxypropyl]amino}carbonyl) -3-(4-fluorophenyl)-5-methyl-1H-pyrrol-2-yl]methylene}-Nisopropyl-2-oxo-2,3-dihydro-1H-indole-5-carboxamide

16S F HO HN O H

(3Z)-3-{[4-({[3-(diethylamino)-2-hydroxypropyl]amino}carbonyl)-3-(2,4-difluorophenyl)-5-methyl-1H-pyrrol-2-yl]methylene}-2-oxo-N-phenyl-2,3-dihydro-1H-indole-5-carboxamide

Attorney Docket No. 038602-1310

(3Z)-3-{[4-({[3-(diethylamino)-2hydroxypropyl]amino}carbonyl) -3-(2,4-difluorophenyl)-5methyl-1H-pyrrol-2yl]methylene}-N-(2hydroxyethyl)-2-oxo-2,3dihydro-1H-indole-5carboxamide

(32)-3-{[3-(4-cyanophenyl)-4-({[3-(diethylamino)-2-hydroxypropyl]amino}carbonyl)-5-methyl-1H-pyrrol-2-yl]methylene}-N,N-dimethyl-2-oxo-2,3-dihydro-1H-indole-5-carboxamide

4-(4-cyanophenyl)-N-[3-(diethylamino)-2hydroxypropyl]-2-methyl-5-{(Z)-[5-(morpholin-4ylcarbonyl)-2-oxo-1,2dihydro-3H-indol-3ylidene]methyl}-1H-pyrrole-3carboxamide

(3Z)-3-{[3-(4-chlorophenyl)-4-({[3-(diethylamino)-2-hydroxypropyl]amino}carbonyl)-5-methyl-1H-pyrrol-2-yl]methylene}-2-oxo-N-phenyl-2,3-dihydro-1H-indole-5-carboxamide

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Attorney Docket No. 038602-1310

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(3Z)-3-{[3-(4-chlorophenyl)-4-({[3-(diethylamino)-2-hydroxypropyl]amino}carbonyl)-5-methyl-1H-pyrrol-2-yl]methylene}-N-isopropyl-2-oxo-2,3-dihydro-1H-indole-5-carboxamide

225

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5-[(Z)-(5-fluoro-2-oxo-1,2-dihydro-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(2H-tetraazol-2-yl)propyl]-2,4-dimethyl-1H-pyrrole-3-carboxamide

23S CI N OH H OH

5-[(Z)-(5-chloro-2-oxo-1,2-dihydro-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(2H-tetraazol-2-yl)propyl]-2,4-dimethyl-1H-pyrrole-3-carboxamide

24S F F N H OH

N-[2-hydroxy-3-(2H-tetraazol-2-yl)propyl]-2,4-dimethyl-5-{(Z)-[2-oxo-5-trifluoromethoxy)-1,2-dihydro-3H-indol-3-ylidene]methyl}-1H-pyrrole-3-carboxamide

25S F H OH

5-[(Z)-(5-fluoro-2-oxo-1,2-dihydro-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(1H-tetraazol-1-yl)propyl]-2,4-dimethyl-1H-pyrrole-3-carboxamide

26S CI H H

5-[(Z)-(5-chloro-2-oxo-1,2-dihydro-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(1H-tetraazol-1-yl)propyl]-2,4-dimethyl-1H-pyrrole-3-carboxamide

27S FFF N H OH

N-[2-hydroxy-3-(1H-tetraazol-1-yl)propyl]-2,4-dimethyl-5-{(Z)-[2-oxo-5-trifluoromethoxy)-1,2-dihydro-3H-indol-3-ylidene]methyl}-1H-pyrrole-3-carboxamide

28S F N OH H

N-{3-[(2R,6S)-2,6-dimethylmorpholin-4-yl]-2-hydroxypropyl}-5-[(Z)-(5-fluoro-2-oxo-1,2-dihydro-3H-indol-3-ylidene)methyl]-2,4-dimethyl-1H-pyrrole-3-carboxamide

29S CI NOH H OH

5-[(Z)-(5-chloro-2-oxo-1,2-dihydro-3H-indol-3-ylidene)methyl]-N-{3-[(2R,6S)-2,6-dimethylmorpholin-4-yl]-2-hydroxypropyl}-2,4-dimethyl-1H-pyrrole-3-carboxamide

30S FFF N H OH

N-{3-[(2R,6S)-2,6-dimethylmorpholin-4-yl]-2-hydroxypropyl}-2,4-dimethyl-5-{(Z)-[2-oxo-5-(trifluoromethoxy)-1,2-dihydro-3H-indol-3-ylidene]methyl}-1H-pyrrole-3-carboxamide

31S F N H OHO

5-[(Z)-(5-fluoro-2-oxo-1,2-dihydro-3H-indol-3-ylidene)methyl]-N-[(2R)-2-hydroxy-3-(3-methyl-2,5-dioxoimidazolidin-1-yl)propyl]-2,4-dimethyl-1H-pyrrole-3-carboxamide

32S CI H OH O

5-[(Z)-(5-chloro-2-oxo-1,2-dihydro-3H-indol-3-ylidene)methyl]-N-[(2R)-2-hydroxy-3-(3-methyl-2,5-dioxoimidazolidin-1-yl)propyl]-2,4-dimethyl-1H-pyrrole-3-carboxamide

FFF NH H

N-[(2R)-2-hydroxy-3-(3-methyl-2,5-dioxoimidazolidin-1-yl)propyl]-2,4-dimethyl-5-((Z)-[2-oxo-5-(trifluoromethoxy)-1,2-dihydro-3H-indol-3-ylidene]methyl}-1H-pyrrole-3-carboxamide

F H OH O

5-[(Z)-(5-fluoro-2-oxo-1,2-dihydro-3H-indol-3-ylidene)methyl]-N-[(2S)-2-hydroxy-3-(3-methyl-2,5-dioxoimidazolidin-1-yl)propyl]-2,4-dimethyl-1H-pyrrole-3-carboxamide

35S FFF N H OH O

N-[(2S)-2-hydroxy-3-(3-methyl-2,5-dioxoimidazolidin-1-yl)propyl]-2,4-dimethyl-5-{(Z)-[2-oxo-5-(trifluoromethoxy)-1,2-dihydro-3H-indol-3-ylidene]methyl}-1H-pyrrole-3-carboxamide

155

33S

34S

36S 37S 38S ÒН 39S

5-[(Z)-(5-chloro-2-oxo-1,2-dihydro-3H-indol-3-ylidene)methyl]-N-[(2S)-2-hydroxy-3-(3-methyl-2,5-dioxoimidazolidin-1-yl)propyl]-2,4-dimethyl-1H-pyrrole-3-carboxamide

N-[3-(1,1-dioxidothiomorpholin-4-y1)-2-hydroxypropyl]-2,4-dimethyl-5-[(Z)-(2-oxo-1,2-dihydro-3H-indol-3-ylidene)methyl]-1H-pyrrole-3-carboxamide

N-[3-(1,1-dioxidothiomorpholin-4-yl)-2-hydroxypropyl]-5-[(Z)-(5-fluoro-2-oxo-1,2-dihydro-3H-indol-3-ylidene)methyl]-2,4-dimethyl-1H-pyrrole-3-carboxamide

5-[(Z)-(5-chloro-2-oxo-1,2-dihydro-3H-indol-3-ylidene)methyl]-N-[3-(1,1-dioxidothiomorpholin-4-yl)-2-hydroxypropyl]-2,4-dimethyl-1H-pyrrole-3-carboxamide

5-[(Z)-(5-bromo-2-oxo-1,2-dihydro-3H-indol-3-ylidene)methyl]-N-[3-(1,1-dioxidothiomorpholin-4-yl)-2-hydroxypropyl]-2,4-dimethyl-1H-pyrrole-3-carboxamide

5-[(Z)-(5-fluoro-2-oxo-1,2-dihydro-3H-indol-3-ylidene)methyl]-N-[(2S)-2-hydroxy-3-morpholin-4-ylpropyl]-2,4-dimethyl-1H-pyrrole-3-carboxamide

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40S

5-[(Z)-(5-fluoro-2-oxo-1,2-dihydro-3H-indol-3-ylidene)methyl]-N-[(2R)-2-hydroxy-3-morpholin-4-ylpropyl]-2,4-dimethyl-1H-pyrrole-3-carboxamide

5-[(Z)-(5-chloro-2-oxo-1,2-dihydro-3H-indol-3-ylidene)methyl]-N-[(2R)-2-hydroxy-3-morpholin-4-ylpropyl]-2,4-dimethyl-1H-pyrrole-3-carboxamide

5-[(Z)-(5-chloro-2-oxo-1,2-dihydro-3H-indol-3-ylidene)methyl]-N-[(2S)-2-hydroxy-3-morpholin-4-ylpropyl]-2,4-dimethyl-1H-pyrrole-3-carboxamide

5-(5-(Z)-fluoro-2-oxo-1,2-dihydro-indol-3ylidenemethyl)-2,4dimethyl-1H-pyrrole-3carboxylic acid [2hydroxy-3-

([1,2,3]triazolo[4,5-b]pyridin-3-yloxy)-

48S

propyl]-amide
5-(5-(Z)-chloro-2-oxo1,2-dihydro-indol-3ylidenemethyl)-2,4dimethyl-1H-pyrrole-3carboxylic acid [2hydroxy-3-

49S

([1,2,3]triazolo[4,5-b]pyridin-3-yloxy)-propyl]-amide
2,4-(Z)-dimethyl-5-(2-

oxo-5-trifluoromethoxy-1,2-dihydro-indol-3ylidenemethyl)-1Hpyrrole-3-carboxyli c acid [2-hydroxy-3-([1,2,3]triazolo[4,5b]pyridin-3-yloxy)propyl]-amide 5-(5-(Z)-fluoro-2-oxo-1,2-dihydro-indol-3ylidenemethyl) -2,4dimethyl-1H-pyrrole-3carboxylic acid [2hydroxy-3-(3-oxybenzotriazol-1-yl)propyl]-amide 5-(5-(Z)-chloro-2-oxo-1,2-dihydro-indol-3ylidenemethyl) -2,4dimethyl-1H-pyrrole-3carboxylic acid [2hydroxy-3-(3-oxybenzotriazol-1-yl)propyl]-amide 2, 4-(Z) -dimethyl-5-(2oxo-5-trifluoromethoxy-1,2-dihydro-indol-3ylidenemethyl)-1Hpyrrole-3-carboxyli c acid [2-hydroxy-3-(3oxy-benzotriazol-1-yl)propyl]-amide

5. A compound of Formula (Ia):

R⁷ N—CH(R³)-*CR⁴(OH)-CH(R⁵)Z

wherein:

 R^1 , R^3 , R^4 , and R^5 are hydrogen;

 R^2 is fluoro and is located at the 5-position of the indolinone ring; and

Z is morpholin-4-yl; R^6 and R^7 are methyl; and the stereochemistry at the *C is (S).

5 6. A compound of Formula (II):

$$R^7$$
 N
 $CH(R^3)$
 $CR^4(OH)$
 $CH(R^5)Z$
 R^6
 R^6

(II)

wherein:

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10 R is hydrogen or alkyl;

 R^1 is selected from the group consisting of hydrogen, halo, alkyl, haloalkoxy, cycloalkyl, heteroalicyclic, hydroxy, alkoxy, $-C(O)R^8$, $-NR^9R^{10}$ and $-C(O)NR^{12}R^{13}$;

 R^2 is selected from the group consisting of hydrogen, halo, alkyl, trihalomethyl, hydroxy, alkoxy, cyano, $-NR^9R^{10}$, $-NR^9C(0)R^{10}$, $-C(0)R^8$, $-S(0)_2NR^9R^{10}$ and $-SO_2R^{14}$ (wherein R^{14} is alkyl, aryl, aralkyl, heteroaryl and heteroaralkyl);

 R^3 , R^4 and R^5 are independently hydrogen or alkyl;

Z is aryl, heteroaryl, heterocycle, or -NR¹⁵R¹⁶ wherein R¹⁵
and R¹⁶ are independently hydrogen or alkyl; or R¹⁵ and R¹⁶
together with the nitrogen atom to which they are attached from a heterocycloamino group;

 ${\ensuremath{\mathsf{R}}}^6$ is selected from the group consisting of hydrogen or alkyl;

25 R^7 is selected from the group consisting of hydrogen, alkyl, aryl, heteroaryl, and $-C(0)R^{17}$ as defined below;

 ${\ensuremath{\mathsf{R}}^8}$ is selected from the group consisting of hydroxy, alkoxy and aryloxy;

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 $\mbox{\sc R}^9$ and $\mbox{\sc R}^{10}$ are independently selected from the group consisting of hydrogen, alkyl, cyanoalkyl, cycloalkyl, aryl and heteroaryl; or

 R^9 and R^{10} combine to form a heterocycloamino group; R^{12} and R^{13} are independently selected from the group consisting of hydrogen, alkyl, hydroxyalkyl, and aryl; or R^{12} and R^{13} together with the nitrogen atom to which they are attached form a heterocycloamino;

R¹⁷ is selected from the group consisting of alkyl, 10 cycloalkyl, aryl, hydoxy, and heteroaryl; or a pharmaceutically acceptable salt thereof.

7. The compound or salt of claim 6, wherein the compound is selected from the group consisting of:

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Cpd

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45N

45S

Structure

Structure

45N

46S

Name

5-(5-Fluoro-2-oxo-1,2-dihydro-indol-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-hydroxy-3-morpholin-4-yl-propyl)-methyl-amide;

5-((Z)-5-Fluoro-2-oxo-1,2-dihydro-indol-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carboxylic acid ((S)-2-hydroxy-3-morpholin-4-yl-propyl)-methyl-amide; and

5-((Z)-5-Fluoro-2-oxo-1,2-dihydro-indol-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carboxylic acid ((R)-2-hydroxy-3-morpholin-4-yl-propyl)-methyl-amide.

8. A pharmaceutical composition, comprising a compound or salt of claims 1, 2, 3, 4, 5, 6, or 7 and a

pharmaceutically acceptable carrier or excipient.

- A pharmaceutical composition, comprising a compound or salt of claims 5 and a pharmaceutically acceptable carrier
 or excipient.
 - 10. A method for the modulation of the catalytic activity of a protein kinase, comprising contacting said protein kinase with a compound or salt of any one of claims 1, 3, or 6.
 - 11. The method of claim 10, wherein said protein kinase is selected from the group consisting of a receptor tyrosine kinase, a non-receptor tyrosine kinase and a serine-threonine kinase.
- A method for treating or preventing a protein kinase related disorder in an organism, comprising administering a therapeutically effective amount of a pharmaceutical
 composition comprising a compound or salt of any one of claims
 3, or 6 and a pharmaceutically acceptable carrier or excipient to said organism.
- 13. The method of claim 12, wherein said protein
 25 kinase related disorder is selected from the group
 consisting of a receptor tyrosine kinase related disorder, a
 non-receptor tyrosine kinase related disorder and a serinethreonine kinase related disorder.
- 30 14. The method of claim 12, wherein said protein kinase related disorder is selected from the group consisting of an EGFR related disorder, a PDGFR related disorder, an IGFR related disorder and a flk related disorder.

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15. The method of claim 12, wherein said protein

kinase related disorder is a cancer selected from the group consisting of squamous cell carcinoma, astrocytoma, Kaposi's sarcoma, glioblastoma, lung cancer, bladder cancer, head and neck cancer, melanoma, ovarian cancer, prostate cancer, breast cancer, small-cell lung cancer, glioma, colorectal cancer, genitourinary cancer and gastrointestinal cancer.

- 16. The method of claim 12, wherein said protein kinase related disorder is selected from the group consisting of diabetes, an autoimmune disorder, a hyperproliferation disorder, restenosis, fibrosis, psoriasis, von Heppel-Lindau disease, osteoarthritis, rheumatoid arthritis, angiogenesis, an inflammatory disorder, an immunological disorder and a cardiovascular disorder.
 - 17. The method of claim 12, wherein said organism is a human.